

## Empathy by default: Correlates in the brain at rest

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### Abstract

**Background:** Empathy, defined as the ability to access and respond to the inner world of another person, is a multidimensional construct involving cognitive, emotional and self-regulatory mechanisms. Neuroimaging studies report that empathy recruits brain regions which are part of the social cognition network. Among the different resting state networks, the Default Mode Network (DMN) may be of particular interest for the study of empathy since it has been implicated in social cognition tasks. **Method:** The current study compared the cognitive and emotional empathy scores, as measured by the Interpersonal Reactivity Index, with the patterns of activation within the DMN, through the neuroimaging methodology of resting-state functional magnetic resonance. **Results:** Results suggest a significant positive correlation between cognitive empathy and activation of the bilateral superior medial frontal cortex nodes of the DMN. Contrastingly, a negative correlation was found between emotional empathy and the same brain region. **Conclusions:** Overall, this data highlights a critical role of the medial cortical regions of the DMN, specifically its anterior node, for both cognitive and emotional domains of the empathic process.

**Keywords:** Emotional empathy, cognitive empathy, default mode network.

### Resumen

**Empatía por defecto: correlatos en el cerebro en reposo. Antecedentes:** la empatía, definida como la capacidad de acceder y responder al mundo interior de otra persona, es un constructo multidimensional que implica mecanismos cognitivos, emocionales y autorreguladores. Los estudios de neuroimagen informan que la empatía recluta regiones cerebrales que forman parte de la red de cognición social. Entre las diferentes redes de estado de reposo, la Red Neuronal por Defecto (Default Mode Network; DMN) puede ser de particular interés para el estudio de la empatía, ya que ha sido implicada en tareas de cognición social. **Método:** el presente estudio comparó los valores de empatía cognitiva y emocional, medidos por medio del Índice de Reactividad Interpersonal, con los patrones de activación dentro de la DMN, a través de la metodología de neuroimagen por resonancia magnética funcional en estado de reposo. **Resultados:** los resultados sugieren una correlación positiva significativa entre la empatía cognitiva y la activación bilateral de los nodos de la región frontomedial superior de la DMN. En contraste, se encontró una correlación negativa entre la empatía emocional y la misma región del cerebro. **Conclusiones:** en general, estos datos destacan un papel crítico de las regiones corticales mediales de la DMN, específicamente su nodo anterior, para los dominios cognitivo y emocional del proceso empático.

**Palabras clave:** empatía emocional, empatía cognitiva, red neuronal por defecto.

Empathy, defined as a process by which we are able to share and understand the emotional states and cognitive processes of others, has been found to be a multidimensional construct involving a variety of psychological processes (Decety & Jackson, 2004; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009; Cox et al., 2012). There is general consensus that empathy encompasses at least three components: (1) a vicarious emotional reactivity to others' internal states, termed affective empathy, or the ability to mirror the other's emotional experience; (2) the recognition of others' experiences, defined as cognitive empathy, comprising perspective taking, theory of mind, and other cognitive abilities; and (3) a regulatory component, represented by inhibitory mechanisms

necessary for keeping the self-other similarity at a minimal level to avert an emotional overflow. This inhibitory component may be crucial to respond in a supportive way to others' needs (Ickes, 1997; Decety & Jackson, 2004; Jackson, Rainville, & Decety, 2006b; Shamay-Tsoory et al., 2009).

Neuroimaging studies have attempted to elucidate the brain network associated with the different components of empathy (Völlm et al., 2006; Shamay-Tsoory et al., 2009; Cox et al., 2012). For example, cognitive aspects of empathy may involve brain regions such as the medial frontal cortex (Jackson, Brunet, Meltzoff, & Decety, 2006a; Shamay-Tsoory et al., 2009), the temporoparietal junction (Decety & Lamm, 2007), and the superior temporal sulcus (Völlm et al., 2006). However, emotional empathy processes (e.g., emotional contagion; emotional recognition) seem to recruit regions such as the inferior frontal gyrus (Shamay-Tsoory et al., 2009), insula (Lamm & Singer, 2010), amygdala, anterior cingulate, and the orbitofrontal cortex (Decety, 2011). Recently, authors have investigated the relationship between brain activity in the resting state (i.e., resting state networks) and social cognition.

Spontaneous neuronal activity generated under resting conditions allowed the identification of several resting-state networks (Rosazza & Minati, 2011). One of those networks is the Default Mode Network (DMN) which is characterized by a network of brain structures that are more active in the absence of goal-directed behavior, namely: the lateral, inferior, and medial parietal cortex; the medial frontal cortex (MFC); the posterior cingulate cortex along with the precuneus (PCC/pC); and the medial temporal cortex (Mazoyer et al., 2001; Raichle et al., 2001; Greicius, Krasnow, Reiss, & Menon, 2003; Mckiernan, Kaufman, Kucera-Thompson, & Binder, 2003; Buckner, Andrews-Hanna, & Schacter, 2008).

The DMN may be of particular interest for the study of empathy since it has been implicated in social cognition tasks (Schilbach, Eickhoff, Rotarska-Jagiela, Fink, & Vogeley, 2008; Mars et al., 2012). It seems associated with social cognition processes such as self-referential mental activity, internal mentation, differentiation between the own and others' psychological states, mentalizing, and emotional responses (Raichle et al., 2001; Buckner et al., 2008; Sampaio, Soares, Coutinho, Sousa, & Gonçalves, 2014). Meta-analyses of functional magnetic resonance imaging (fMRI) studies have found a significant overlap between the DMN and the set of brain areas previously reported as the social network, as well as a consistent overlap in individual brain regions, such as the temporo-parietal junction, inferior parietal lobes, medial posterior cortex, and the medial wall of the frontal cortex (Schilbach et al., 2008; Mars et al., 2012).

Given the current evidence for the association between DMN activity and several social cognition processes involved in empathy, we may anticipate that different patterns of DMN activity are associated with aspects of the empathic experience. The objective of this study is to investigate the relationship between cognitive and emotional empathy scores and activation patterns within the DMN. Building on data from previous neuroimaging studies, we expect a positive correlation between the medial frontal cortex DMN node and individual scores in the cognitive subscale of empathy. Additionally, we anticipate a positive correlation between the PCC/pC node of the DMN and individual scores in the emotional subscale of empathy.

## Methods

### Participants

Ten Portuguese right-handed subjects aged between 24 and 37 years (women's mean (SD) = 29.4 (4.5); men's mean (SD) = 30.2 (4.6); 50% women) volunteered for this study. Participants were recruited through a subject pool of college students and from the local community. Before participation, all participants signed an informed consent. The study was approved by the internal ethical committee, namely the Centro de Investigação em Psicologia. No participant reported a history of neurological or psychiatric disease, substance use disorder, or the use of psychoactive medication.

### Instruments

*Empathy self-report measure.* The Interpersonal Reactivity Index (IRI; Davis, 1983) was used to allow the measure of both cognitive and affective dimensions of empathy. The IRI has four

subscales: 'IRI-PT' - Perspective Taking (measure of how often subjects spontaneously assume the point of view of others); 'IRI-EC' - Empathic Concern (measure of other-oriented feelings of compassion when facing negative experiences); 'IRI-PD' - Personal Distress (self-oriented measure of personal anxiety resulting from interpersonal relationships); and 'IRI-FS' - Fantasy (measure of one's ability to project the self into the position of fictional personages) (Davis, 1983). The IRI allows the assessment of two key components of empathy, namely, the cognitive and emotional dimensions. The IRI-PT subscale is described as assessing the cognitive domain of empathy, whereas the other three subscales (i.e., IRI-EC, IRI-PD, and IRI-FS) are related to the affective/emotional domain (Davis, 1983). Only two subscales of the IRI were used in the present study, the IRI-PT (to assess cognitive empathy) and the IRI-EC (to assess emotional empathy).

### Procedure

Upon arrival, participants observed a computerized presentation describing the study (including informed consent, the questionnaires administration, and the scanning procedure). After signing the informed consent form and completing the demographic, handedness preference (Edinburgh Handedness Inventory; Oldfield, 1971), and the IRI questionnaires, participants were invited into the scanner.

*fMRI data acquisition.* The fMRI scanning session was conducted on a clinically approved 3T MRI system (Achieva 3.0T Philips Medical Systems, Netherland) equipped with a gradient booster, a standard eight-channel head coil, and the capacity to control for head movement. For resting-state acquisition, T2\*-weighted echo planar images were acquired in a single run, using the following parameters: 100 volumes, 45 transversal axial slices, repetition time = 3 s, time echo = 40 ms, field of view = 235 mm, flip angle = 90°, acquisition matrix = 72 × 74; voxel size = 3×3×3 mm<sup>3</sup> with no gap. The resting state measurement was performed during resting wakefulness. Participants were explicitly instructed to relax, move as little as possible, and keep their eyes closed in one run of five minutes. After the scanning sessions, participants were debriefed about how they felt during the experiment, and about the objectives of the study.

### Data analysis

Before preprocessing, data were examined to exclude brain lesions or critical head motion. To allow participants to adapt to the scanning environment and enable the signal to reach a steady state, the first 6 volumes (18 s) of each participant were removed from the analysis. During the scans, the range of movement was less than 1.5 mm of translation and 1.5 degrees of rotation in any direction.

*Preprocessing.* fMRI preprocessing was carried out using the Data Processing Assistant for Resting-State fMRI (DPARSF; Chao-Gan & Yu-Feng, 2010, <http://www.restfmri.net/forum/DPARSF>). The procedure followed conventional methods described by Sampaio et al. (2014). The slice-timing correction was performed to correct for differences in acquisition times due to interleaved acquisition, realigning all images to the first slice acquired (i.e., used as a reference slice) and applying the SPM8 (Statistical Parametric Mapping 8 - <http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>) Fourier phase shift interpolation. Head

motion was corrected through the realignment of each input image to the mean image (i.e., the target image), using a rigid body transformation. Afterwards, the fMRI data were spatially normalized to the standardized stereotaxic space Montreal Neurological Institute template and the normalized volumes were spatially resampled to a  $3 \times 3 \times 3$  mm<sup>3</sup> voxel size using sinc interpolation. This step was performed using an isotropic FMHM Gaussian Kernel of 8mm, following a linear trend removal and filtering process to ensure the removal of low and high-frequency physiological noise (through a 0.01 - 0.08 Hz band-pass temporal filter).

**Group Independent Component Analysis (ICA).** Once the preprocessing step was completed, resting-state scans were combined and analyzed using Independent Component Analysis (the Group ICA approach; Calhoun, Adali, Pearlson, & Pekar, 2001) by the GIFT software implemented in Matlab. Preprocessed data were concatenated and reduced to one group, allowing an estimate of independent group components using the Infomax algorithm (Bell & Sejnowski, 1995). Additionally, 20 spatially independent components, based on the trade-off between preserving the information in the data while reducing its size (Beckmann, DeLuca, Devlin, & Smith, 2005; Zuo et al., 2010), were predefined for each subject in order to split the resting-state fMRI dataset into independent functional networks (Franco, Pritchard, Calhoun, & Mayer, 2009). The spatial maps and temporal profiles of the subjects' individual components were computed through the group ICA using the ICASSO algorithm. To assess the ICA reliability, 10 computational runs were performed on the dataset with a convergence threshold of  $1 \times 10^{-6}$  (Himberg, Hyvärinen, & Espósito, 2004; Van De Ville et al., 2012). For each subject, the back-reconstructed, independent components spatial maps were computed and converted to z-scores. Signal variation and alignment were considered as the units resulting from ICA analysis are arbitrary (Beckmann et al., 2005). Components related to artifacts were discarded based on visual inspection and a frequency analysis of the estimated IC. The DMN of each participant was selected using visual inspection and a spatial correlation with the template of the DMN supplied in GIFT (Calhoun et al., 2001; Franco et al., 2009). Individual subject's best-fit IC spatial map corresponding to the DMN was used to perform second-level analyses on SPM8.

Voxel-wise statistical parametric maps from the analysis were given a DMN mask and entered into a 2nd level random-effect group analysis, using a one sample T-test. A multiple regression was performed using IRI parameters as covariates of interest. The distinct anatomical areas were defined by visual inspection and the Anatomical Automatic Labeling atlas (Tzourio-Mazoyer et al., 2002). Results were considered significant after threshold adjustment, based on the Monte Carlo simulation, using the AlphaSim command implemented in the REST software, [http://restfmri.net/forum/REST\\_V1.8](http://restfmri.net/forum/REST_V1.8)). This corrected all statistical results for multiple comparisons. The correction resulting from 5,000 iterations of the Monte Carlo simulation yielded a probability of  $\alpha = 0.05$ , a voxel wise probability threshold of  $p < 0.01$  combined with a minimum cluster size of 48 voxels.

## Results

**Self-report data.** Responses were computed separately for each subscale, resulting in two scores: IRI-PT representing the

cognitive score, and IRI-EC representing the emotional score. Participant's scores on the IRI-PT ranged from 10 to 24 ( $M = 17.30$ ,  $SD = 4.69$ ), and on the IRI-EC from 10 to 20 ( $M = 16.70$ ,  $SD = 3.53$ ). Pearson and point-biserial correlations were calculated to assess the relationship between age and gender and the empathy subscales, specifically IRI-PT (age:  $r = -.079$ ,  $p = .829$ ; sex:  $r_{pb} = .427$ ,  $p = .219$ ), and IRI-EC (age:  $r = -.403$ ,  $p = .248$ ; sex:  $r_{pb} = -.09$ ,  $p = .806$ ), and no significant associations were found. All statistical analyses were performed using the IBM SPSS Statistics software (v20). A summary of participants' IRI scores by gender is provided in Table 1.

**DMN results.** The independent components extracted from each subject were used to perform group-level analysis (a one-sampled *t*-test with a threshold set at  $p < .05$ , Monte Carlo-corrected, as shown in Figure 1). Based on an ICA of resting-state fMRI data from all subjects, increased activation was found in the medial prefrontal area, precuneus, and bilateral parietal cortex. The coordinates and Z scores for the DMN areas are described in Table 2.

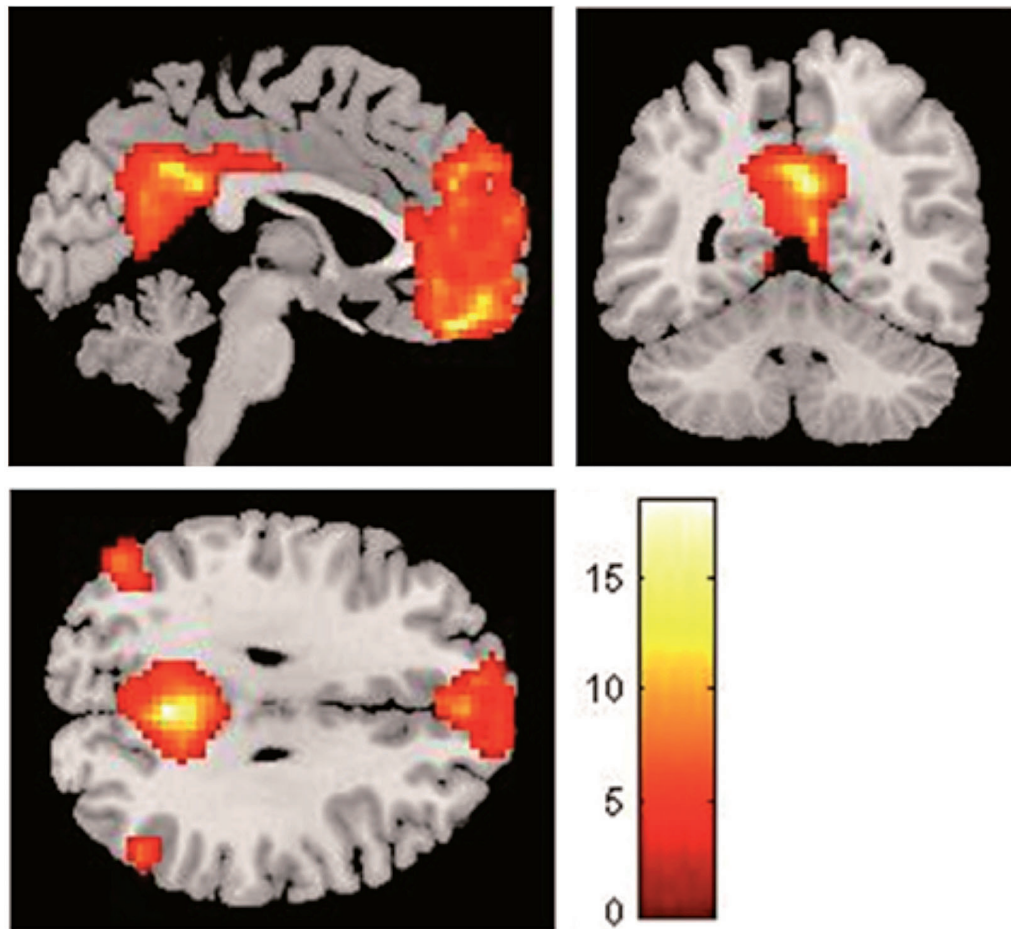
When age, sex, and the alternate IRI subscale were entered the model as covariates, cognitive subscale scores (i.e., IRI-PT scores) were positively correlated with activation of the superior medial frontal cortex bilaterally ( $x = -3$ ,  $y = 42$ ,  $z = 21$ ,  $T = 10.01$ ,  $IC = 0.16$ - $0.22$ ). In other words, cognitive scores were associated with functional connectivity in the superior medial frontal cortex in both hemispheres. Interestingly, emotional subscale scores (i.e., IRI-EC scores) were inversely correlated with the same brain region (right:  $x = 12$ ,  $y = 60$ ,  $z = 9$ ,  $T = 6.17$ ,  $IC = 0.17$ - $0.29$ ; left:  $x = -18$ ,  $y = 51$ ,  $z = 27$ ,  $T = 12.81$ ,  $IC = 0.15$ - $0.20$ ). Overall, higher scores in the emotional subscale were associated with low levels of connectivity in the bilateral superior medial frontal cortex (see Table 3 and Figure 2).

*Table 1*  
Demographic data and IRI subscales scores by gender

Demographic data		IRI's subscales scores	
Sex	Age (years) <sup>a</sup>	Cognitive empathy (IRI-PT) <sup>b</sup>	Emotional empathy (IRI-EC) <sup>c</sup>
Women	5	29.4 (4.5)	15.4 (4.9)
Men	5	30.2 (4.6)	19.2 (4.1)
Total		29.8 (4.3)	17.3 (4.7)
Notes: <sup>a</sup> Mean (Standard Deviation); IRI: Interpersonal Reactivity Index; <sup>b</sup> IRI-PT: subscale Perspective Taking; <sup>c</sup> IRI-EC: subscale Empathic Concern			

*Table 2*  
Group statistics of the DMN activation (FEW < .05 corrected, extent threshold  $k = 10$  voxels)

Brain region	Maximum Z score	Cluster size (voxels)	Peak MNI coordinates		
			x	y	z
Precuneus	5.62	808	0	-54	30
Medial prefrontal	5.62	2083	0	48	-21
Right parietal lobe	5.21	134	51	-63	33
Left parietal lobe	4.23	146	-51	-69	33
Note: Coordinates are in MNI space					



**Figure 1.** The DMN identified in the resting state condition at the group level ( $p < .05$ , FWE corrected)

*Table 3*

DMN Clusters and IRI's cognitive and emotional subscales (k - cluster size, MNI peak coordinates displayed - x, y, z)

	MNI coordi- nates x, y, z	Cluster size (voxels)	Maximum Z score	95 % CI
<i>Brain areas positively correlated with cognitive empathy (IRI-PT)</i>				
Bilateral superior medial frontal	-3, 42, 21	119	3.76	0.16 to 0.22
<i>Brain areas negatively correlated with emotional empathy (IRI-EC)</i>				
Bilateral superior medial frontal	-18, 51, 27 12, 60, 9	59	4.05 3.15	0.15 to 0.20 0.17 to 0.29

*Notes:* IRI-PT: Perspective Taking, cognitive subscale of the Interpersonal Reactivity Index (IRI; Davis, 1983); IRI-EC: Empathic Concern, emotional subscale of the IRI

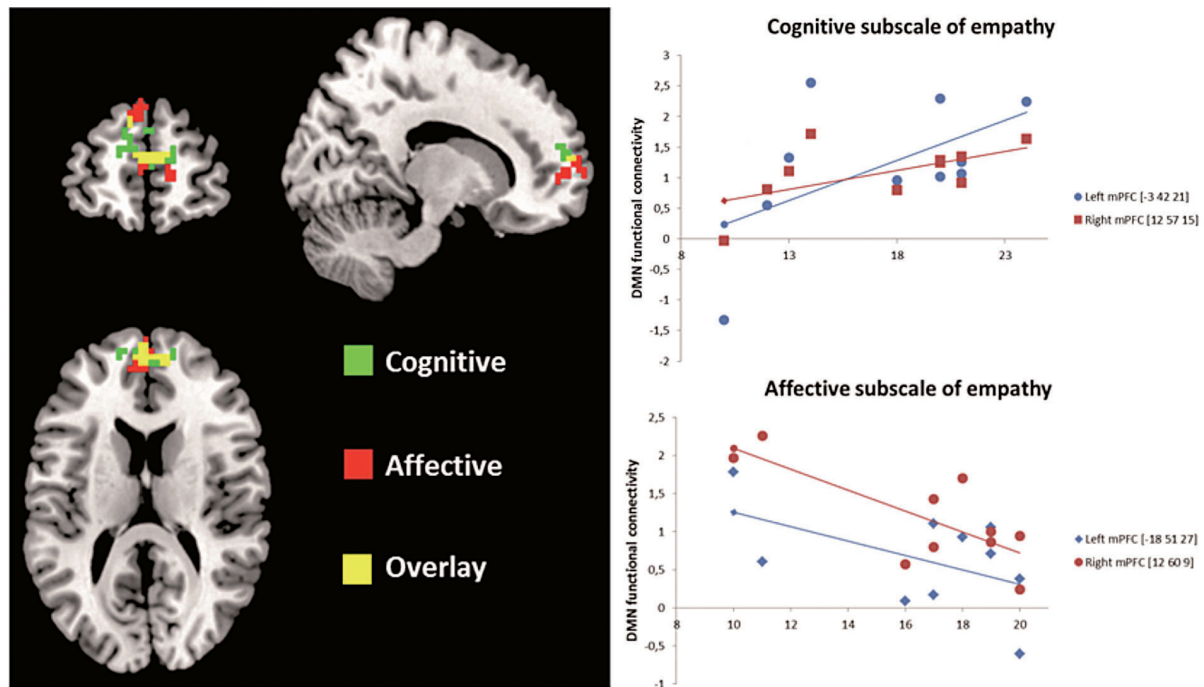
## Discussion

In this study, we predicted that individuals with high scores in the cognitive empathy subscale of the IRI would manifest functional activation of the anterior DMN regions, namely the medial prefrontal cortex (MPFC). In addition, we predicted that high scores in the emotional empathy subscale would

be associated with functional connectivity in the posterior DMN regions, particularly the PCC/pC. Our findings partially supported these hypotheses. Regarding the first hypothesis, we found a significant positive correlation between IRI-PT scores and functional activation in the superior medial frontal cortex bilaterally.

However, our second hypothesis was not supported. Interestingly, we found an unpredicted negative correlation between subjects' scores in emotional empathy and activation in the medial frontal cortex. These results highlight the crucial role of the medial frontal regions in managing cognitive and emotional domains during interpersonal interactions to produce a consistent empathic experience, suggesting a potential involvement of this brain area in reciprocal modulation of these two dimensions of empathy. Similar findings of the reciprocal modulation between cognition and emotion have been previously reported in studies using focused attention tasks. Drevets and Raichle (1998) reviewed evidence from regional cerebral blood flow studies and reported that cognitive performance can suppress the activity of emotion-related brain areas, such as when patients with depression report less psychological and somatic symptoms when engaged in cognitively demanding activities. The same authors report that emotional activation can interfere with the activation of brain areas associated with cognitive functions, deteriorating cognitive performance.





**Figure 2.** On the left, DMN regions positively correlated with cognitive empathy (in green) and negatively correlated with emotional empathy (in red), as measured by IRI (Interpersonal Reactivity Index). To allow the discrimination of the precise location and extent of each cluster, the overlap between brain regions involved in both positive and negative correlations is shown in yellow. For all the correlations, the  $p < .05$  (corrected for multiple comparisons). On the top right, the graph shows the positive correlation between the individual cognitive scores of empathy and the DMN components. On the bottom right, the graph shows a negative correlation between the individual emotional scores of empathy and the DMN components. MPFC = medial prefrontal cortex

Empathy involves self-regulatory mechanisms which allow the establishment of boundaries between the self and others (Hoffman, 1984; Decety & Jackson, 2004). When emotional activation triggered by exposure to others' feelings is not properly managed, an emotional overload may result, compounded by personal distress, concern for the other's distress, and the desire to alleviate both. The brain mechanisms responsible for regulating emotional reactivity may have a key role in the empathic process by establishing a distinction between other and self-related feelings (Decety & Svetlova, 2012). Indeed, prefrontal areas of the brain and the cingulate system have been typically implicated in emotion regulation (Ochsner & Gross, 2005).

The pattern of resting-state functional activation is thought to be particularly useful for the characterization of intrinsic functional organization and individual differences in the brain (Fox & Raichle, 2007). One potential interpretation of our results is that the distinctive patterns of association between the medial frontal cortex and self-reported empathy scores are mediated by regulatory mechanisms necessary for providing top-down control of emotional processing. One may speculate that subjects with stronger activation of the medial frontal areas may be more prone to gain control over feelings evoked by other's distress, thus using cognitive resources to adopt the other's perspective, which in turn produces high scores in cognitive empathy. On the other hand, those subjects who are not able to modulate efficiently between other-focused and self-focused processes might have lower activation of medial frontal areas (i.e., the brain area underpinning executive control) and become more vulnerable to the other's suffering, reporting higher scores in the emotional empathy subscale. The

close relationship between empathy and executive regulatory mechanisms is critical not only to reduce personal distress in response to others' distress, but also to attenuate a dominant self-perspective. Although self-perspective is considered an important source of influence for the process of understanding others' internal states (Gilovich, Medvec, & Savitsky, 2000). The spotlight effect in social judgment: an egocentric bias in estimates of the salience of one's own actions and appearance (Gilovich, Medvec, & Savitsky, 2000) and the empathic process (Decety & Jackson, 2006), failure to restrain salient self-related information may negatively impact our ability to access another's inner experience (Ruby & Decety, 2003).

As mentioned previously, one of our hypotheses was not confirmed. Considering the functions associated with the posterior nodes of the DMN, namely the non-valence-specific interface between emotion and episodic memory (Maddock, Garrett, & Buonocore, 2003), as well as their modulatory effect on the autonomic system (Shin et al., 2013), we expected that individual emotional empathy scores would be associated with activation in those areas. The failure to provide this evidence may result from the negative content of items in the emotional empathy subscale. These might summon the activation of brain regions which process negative emotions and self-regulatory mechanisms – such as areas within the frontal node of the DMN – rather than those which retrieve episodic memory for emotional contexts.

Finally, although these results are consistent with findings from previous studies, some limitations of this study need to be addressed. Firstly, no causal relationships can be extrapolated

despite strong evidence that measures of empathy and activation in the DMN are linked. Secondly, our methodological choice regarding the DMN acquisition approach (i.e., a task-free sequence rather than a task-related deactivation paradigm) should be considered as a limit to generalizability. The choice of the DMN task-free approach was made to avoid the potential confounding effects of any task-related deactivation. Future studies ought to evaluate whether similar results will be obtained with task-related deactivation approach. In conclusion, our results suggest a pivotal involvement of the frontal node of the DMN, more specifically

the MPFC, in the cognitive and emotional aspects of the empathic experience.

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